

Remarks

Claims 1-14, 18-34 and 36 are pending in the present application. No new matter has been added.

I. Rejections Under 35 U.S.C. § 112, first paragraph

A. *Enablement*

The Examiner maintains the rejection of claims 1-14, 18-34 and 36, under 35 U.S.C. § 112, first paragraph, as allegedly containing “subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” *See*, Paper No. 112003, pages 2-5. The rejection is respectfully traversed.

Specifically the Examiner alleges that:

the Specification as filed does not teach or suggest the use of the claimed polynucleotide in detecting the hPSP polypeptide in primary colon tumors. The passages pointed by the Applicant (*sic*) only generally disclosed ... assaying hPSP gene expression level, whereby an increase or decrease in the assayed hPSP gene expression level is indicative of disorder ... [t]he specification does not disclose any diseases or conditions known to be associated with the hSLAP (*sic*) polypeptide, encoded by SEQ ID NO:2 or any conditions associated with altered levels (increase or decrease (*sic*)) of said polypeptide.

See, Paper No. 112003, page 3. Applicants respectfully disagree and contend that the instant specification teaches that the claimed polynucleotide may be used to detect hPSP polypeptide expression in diagnosis of cancer including colon tumors. For example, in the specification at page 33, lines 15-23, Applicants teach that “the invention provides a diagnostic method useful during diagnosis of a digestive, nonimmune defense, endocrine or immune system disorder, including cancers of these systems, which involves measuring the expression level of the gene encoding the hPSP protein.” In this single disclosure the

specification has taught that the present invention can be used to diagnose digestive diseases and cancers of the digestive system. The colon being a widely accepted part of the digestive system, one of ordinary skill in the art would have understood the above disclosure to indicate the usefulness of the invention in diagnosing digestive diseases and tumors including colon cancer.

Furthermore the instant specification does more than “only generally disclose” the use of the present invention in diagnosing disease by measuring levels of expression of hPSP. As of the filing date of the instant application measurement of the expression level of a given polypeptide was a routine matter. For example, the specification teaches that use of a claimed nucleic acid as a nucleotide primer was routine and well within the abilities of those of ordinary skill in the relevant arts on the priority date of the present invention. *See e.g.*, Page 43, lines 8-19; Page 44, lines 16-29; Page 47, line 25 to Page 48 line 2; and Page 31, line 13 through page 32, line 16. Accordingly, one of skill in the art in possession of the instant specification would have had to carry out only routine experimentation in order to use the present invention in the diagnosis of diseases and conditions including colon tumors.

Furthermore, the Examiner alleges that:

[t]here does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various nucleic acids recited in the instant claims. A person of skill in the art would not know which sequences are essential and which sequences are non-essential ... There is insufficient guidance as to which nucleic acid residue within the nucleic acid sequence mention above (*sic*) or amino acid sequence within a polypeptide encoded by amino acid sequence of SEQ ID NO:2 are *essential for the functional properties of nucleic acid molecule or the encoded polypeptide*.

See, Paper No. 112003, page 4 (*emphasis in original*). Applicants respectfully disagree and traverse this basis for rejection.

It is well settled that the test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 8 U.S.P.Q. 2d 1217 (Fed. Cir. 1988).

Once more Applicants' respectfully point out that the nucleic acids of the invention have several uses asserted in the specification, including use as an agent that hybridizes to other polynucleotides, (*e.g.*, a primer or a probe). One of skill in the art would be capable of routinely using a polynucleotide of the claimed invention for such a purpose. For example, one or more claimed polynucleotides may be used in the diagnosis of diseases of the digestive system and the non-immune defense of gastrointestinal mucosal surfaces. *See e.g.*, specification at Page 5, lines 28-32; Page 8, lines 27-30; Page 9, lines 22-28; and Page 32, line 20 through Page 37, line 12. Furthermore, it is not necessary for the claimed polynucleotides, or any polypeptides encoded thereby, to be "biologically active" or to be defined by "functional properties," in order for them to be fully enabled for such a use, and therefore the Examiner's reliance on the teachings of Skolnick *et al* and Ngo *et al* is misplaced. In such a use of the invention, the only "functional" attribute necessary of a claimed polynucleotide is that it be capable of hybridization to SEQ ID NO:1 of the instant specification. Furthermore, the hybridization arts were among the most predictable in biology on the priority date of the present invention. Accordingly, use of the claimed nucleic acids in such a manner was routine and well within the abilities of those of ordinary skill in the relevant arts on the priority date of the present invention. *See e.g.*, specification at Page 43, lines 8-19; Page 44, lines

16-29; Page 47, line 25 to Page 48 line 2; and Page 31, line 13 through page 32, line 16. Therefore, Applicants contend that one of ordinary skill in the art would have been able to routinely use the nucleic acids commensurate with the scope of the claims.

Accordingly, Applicants assert that one reasonably skilled in the art, armed with the disclosure in the present specification coupled with information known in the art at the time the application was filed, could make and use the claimed polynucleotides, without undue experimentation. Therefore the claimed polynucleotides are fully enabled within the meaning of 35 U.S.C. §112.

Furthermore, under 35 U.S.C. § 112, an inventor is not required to disclose "a test of every species encompassed by their claims," even in an unpredictable art. *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976) (emphasis in original). Enablement is not precluded even if some experimentation is necessary. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1376, 1384 (Fed. Cir. 1986). This is so even if the amount of experimentation required is laborious. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). Furthermore enablement is not precluded even if some embodiments of the claimed invention are inoperative. Indeed, the M.P.E.P. states that "[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. *See*, M.P.E.P. § 2164.08(b).

Applicants assert that the Examiner has underestimated the level of skill of the skilled artisan and the teachings of the present specification. The skilled molecular biologist, enlightened by the teaching of the present specification, is more than capable of routinely determining whether a polynucleotide encompassed by the claims has uses commensurate in scope with the instant claims.

In view of the above remarks, Applicants believe the Examiner's concerns have been fully addressed. Accordingly, Applicants respectfully request reconsideration and

withdrawal of the rejection of claims 1-14, 18-34 and 36, under 35 U.S.C. § 112, first paragraph, for lack of enablement.

B. *Written Description*

The Examiner maintains the rejection of claims 1, 5, 9-14, 18-20, 26-34 and 36, under 35 U.S.C. § 112, first paragraph, as allegedly “containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” *See*, Paper No. 112003, pages 5-7. More specifically the Examiner states:

The specification fails to provide sufficient guidance as to which core structure of SEQ ID NO:1 is essential to maintain its functional activity and which changes can be made in the structure of SEQ ID NO:1 and still maintained the same function ... there is insufficient description or art-recognized correlation or relationship between the structure of the invention, the nuclei (*sic*) acid sequence of SEQ ID NO:1 that encodes polypeptide hPSP of SEQ ID NO:2 and it's (*sic*) function that is essential to the instant invention.

See, Paper No. 112003, page 6, lines 6-8 and lines 28-31.

Applicants respectfully disagree with the Examiner and submit that one skilled in the art could reasonably conclude that Applicants had possession of the polynucleotides encompassed by the rejected claims, in the present application as filed. Furthermore, Applicants submit that the Examiner has underestimated both the teaching of the present application and the level of skill in the art on the priority date of the present application.

Preliminarily, Applicants respectfully point out that functional activity of a polypeptide is not a prerequisite of the present invention. One of skill in the art would appreciate that use of the instant invention requires that the claimed polynucleotide be capable of hybridization to a reference nucleotide sequence and does not require any further structural or functional characterization. Accordingly, provision of the nucleotide

sequence of SEQ ID NO:1 is, in and of itself, a sufficient written description of the instant invention.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. The Federal Circuit recently re-emphasized the well-settled principle of law that “[t]he written description requirement does not require the applicant ‘to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed,’” *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000). Further, the Federal Circuit has emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification; and not whether the specific embodiments had been explicitly described or exemplified. Indeed, the court noted that “the issue is whether one of skill in the art could derive the claimed ranges from the patent’s disclosure.” *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000) (emphasis added).

It is well established that a “gene is a chemical compound, albeit a complex one”. *Amgen, Inc. v. Chugai Pharmaceutical Co., LTD.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, the claims of the instant application, directed to particular polynucleotides of the disclosed nucleic acid sequence of SEQ ID NO:1, are essentially chemical claims involving generic chemical formulae. As stated by Judge Lourie in *University of California v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997), “In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims

encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.” All of the objectives met by a generic chemical formula are similarly met by the explicit description in the instant specification of a polynucleotide sequence (*i.e.* SEQ ID NO:1) and the amino acid sequence encoded thereby (SEQ ID NO:2). Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polynucleotides encompassed by the rejected claims upon reading the present application as filed, and would immediately recognize that the Applicants had “invented what is claimed” (*Vas-Cath*, 935 F.2d at 1563). Therefore, the specification contains an adequate written description of the claimed polynucleotides. Applicants have provided the skilled artisan with a “generic formula” in the form of the nucleic acid sequence of SEQ ID NO:1, which indicates “with specificity what the generic claims encompass.” Armed with this information “one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass.” Moreover, Applicants submit that one skilled in the art would be able to “visualize and recognize” innumerable members of the genus given the disclosure of the reference sequence common to all members of the genus. Indeed, the Written Description guidelines state:

if an applicant disclosed an amino acid sequence, it would be unnecessary to provide an explicit disclosure of nucleic acid sequences that encoded the amino acid sequence. Since the genetic code is widely known, a disclosure of an amino acid sequence would provide sufficient information such that one would accept that an applicant was in possession of the full genus of nucleic acids encoding a given amino acid sequence.

See, M.P.E.P. § 2163(II)(A)(3)(a)(ii) at 2100-165. Thus Applicants assert that the specification has satisfied the requirements for written description as set forth in *Eli Lilly & Co.* Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Examiner appears to allege that Applicants are not in possession of a single polynucleotide sequence at least 95% identical to: (a) a polynucleotide encoding the amino acid sequence of SEQ ID NO:2; (b) a polynucleotide encoding the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 97811; (c) the nucleic acid sequence of SEQ ID NO:1; (d) the nucleic acid sequence of the cDNA contained in ATCC Deposit No. 97811; or (e) a polynucleotide encoding any one of the listed N- or C-terminal deletions of the amino acid sequence of SEQ ID NO:2 or of the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 97811. Applicants submit that the specification as filed contains abundant written description to support claims drawn to a polynucleotide at least 95% identical to each polynucleotide explicitly disclosed in the present application. Explicit written support for polynucleotides sharing at least 95% identity may be found, for example, at Page 7, lines 1-23; at Page 18, line 1 to Page 20, line 16; and at Page 28, line 19 to Page 29, line 2. Additionally, the specification provides detailed teachings on methods used to determine the sequence identity shared by two or more polynucleotides (*See* Page 18, line 20 to Page 19, line 10). Furthermore, as discussed above, it is not necessary to conserve a functional attribute of an encoded polypeptide when identifying such a polynucleotide sharing 95% identity, as the sole structural necessity of the claimed polynucleotides is precisely their degree of relationship to the reference nucleotide sequence and their usefulness in detecting that reference nucleotide sequence by hybridization.

Further embodiments of the invention, rejected by the Examiner in the present action and fully described in the specification as filed, include: (a) epitope-bearing portions of hPSP, which are described, for example, at Page 31, lines 1-13; (b) recombinant vectors and host cells comprising a polynucleotide of the invention as well as

methods for making them, which are described, for example, at Page 20, line 17 to Page 22, line 28; and at Page 43, line 34 to Page 54, line 19; (c) polynucleotides identical to or at least 95% identical to at least 30 contiguous nucleic acid residues of a polynucleotide of the invention which are described, for example, at Page 15, lines 9-31; (d) polynucleotides comprising SEQ ID NO:1, or a polynucleotide encoding a mature hPSP polypeptide, or a polynucleotide identical to the cDNA contained in ATCC Deposit No. 97811, or a polynucleotide encoding at least 30 contiguous amino acids of hPSP, or a polynucleotide complementary to any of the claimed nucleic acid sequences, which are described, for example, at Page 5, line 34 to Page 6, line 1; at Page 6, lines 6-9; at Page 7, lines 1-17; at Page 8, lines 15-24; at Page 12, line 20 to Page 14, line 2; and at Page 16, lines 3-18; (e) a polynucleotide of the invention further comprising a heterologous polynucleotide, which may or may not encode a heterologous polypeptide, which are described, for example, at Page 20, line 30 to Page 21, line 20; at Page 21, lines 26-28; at Page 32, lines 5-17; at Page 43, line 35 to Page 46, line 32; and at Page 49, line 26 to Page 54, line 19; and (f) a composition comprising a polynucleotide encoding SEQ ID NO:2, the amino acid sequence encoded by the cDNA of ATCC Deposit No.97811, or at least 30 contiguous amino acid residues of SEQ ID NO:2, which are described, for example, at Page 5, line 34 to Page 6, line 1; at Page 6, lines 6-9; at Page 7, lines 1-17; at Page 8, lines 15-24; at Page 12, line 20 to Page 14, line 2; at Page 15, lines 9-31; at Page 16, lines 3-18; at at Page 20, line 17 to Page 22, line 28; at Page 32, lines 5-17; and at Page 43, line 34 to Page 54, line 19. Accordingly, one skilled in the art, enlightened by the teachings of the present application, could readily envision all of the various polynucleotide sequences that comprise the specified polynucleotides as rejected by the Examiner.

In regard to the Examiner's contention that "one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants" Applicants respectfully disagree. The present application describes the human parotid secretory protein (hPSP) and the polynucleotides which encode it as well as variants and derivatives thereof. Applicants contend that the disclosure of structural features which are common to every member of the genus ensures that one skilled in the art could readily envision the claimed polynucleotide sequences, and therefore the written description requirement of 35 U.S.C. § 112, first paragraph, has been met. For example, the skilled artisan could clearly envision each of the polynucleotides comprising at least 30 contiguous nucleotides of SEQ ID NO:1 as a progression, *i.e.*, polynucleotides comprising nucleotides 1-30, 2-31, 3-22, etc. The skilled artisan could certainly further envision sequentially adding contiguous nucleotides to either end of any of the described embodiments. Indeed, nothing more than what is described in the specification would be required for the skilled artisan to identify every single one of the polynucleotides and polynucleotide fragments containing at least 30 nucleotides of SEQ ID NO:1. Likewise, the skilled artisan could easily substitute any given nucleotide for any other given nucleotide, or add or delete nucleotides, such that nothing more than what is described in the specification would be required to identify every single one of the polynucleotides comprising nucleotide sequences that are at least 95% identical to the nucleotide sequence of SEQ ID NO:1. Furthermore, the skilled artisan could easily substitute any given codon for any other given codon encoding the same amino acid residue, or add or delete codons, such that nothing more than what is described in the specification would be required to identify every single one of the polynucleotides encoding at least 30 and/or at least 50 amino acid residues of the amino acid sequence of SEQ ID NO:2. Thus, it would be readily apparent to the skilled artisan that the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563).

For all of the above reasons, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

In light of these clarifications, Applicants respectfully request that the Examiner's rejection of claims 1, 5, 9-14, 18-20, 26-34 and 36, under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the remarks of the present response be entered and made of record in the present application. The present application is believed to be in condition for allowance. Early notice to that effect is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below. If a fee is required in connection with this paper, please charge Deposit Account No. 08-3425 for the appropriate amount.

Respectfully submitted,

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